

REMARKS

Claims 1 and 7 are amended herein, claims 2 and 12 are canceled, and claim 15 is newly added.

The examiner rejects claims 1-6 and 12 under 35 USC §112, ¶1 for lack of enablement and lack of adequate written description. Applicants have amended claim 1 to introduce a requirement that the functional variants, analogues or derivatives share at least 50% homology with the identified biotin biosynthesis genes. New claim 15 is drawn to similar subject matter, with the exception that it claims combination with additional biotin biosynthesis genes, not necessarily possessing at least 50% homology with the identified sequences. The specification clearly indicates that a number of other enzymes are known to have the ability to assume the enzymic activity of bioS1, bioS2 or bioS3 in the synthesis of biotin (p.5:23-29). Given the relatively broad range of genes *known* in the art to be suitable substitutes, the ability of one of skill in the art to recognize and use functional equivalents is relatively high. Accordingly, the homology range now recited in claim 1 is enabled, and the above citation to the specification indicates that adequate written description is provided. Applicants respectfully request that the rejections under 35 USC §112, ¶1 be withdrawn.

With regard to the double patenting rejection, claim 1 of US 6,436,681 to Schröder recites use of two sequences *in the alternative*, using a Markush grouping.

The claims are not drawn to a process involving use of *both* sequences together, as in the present claims. Accordingly, no double patenting is possible in the present application. Should the examiner, however, disagree with this point, the claim

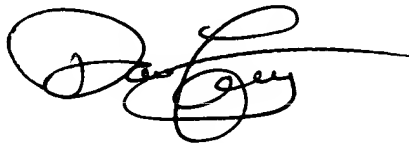
SCHROEDER, Serial No. 09/622,419

amendments should be sufficient to overcome any lingering concerns.

In view of the foregoing amendments and remarks, applicants consider that the rejections of record have been obviated and respectfully solicit passage of the application to issue.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,  
KEIL & WEINKAUF

A handwritten signature in black ink, appearing to read 'David C. Liechty', with a long horizontal flourish extending to the right.

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**COPY OF ALL CLAIMS**

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1. (currently amended) A process for producing biotin wherein an

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S-adenosylmethionine synthase gene, having the sequence SEQ ID No. 1, and at least one further biotin biosynthesis gene bioS1, bioS2 or bioS3, having the sequences SEQ ID No. 3, SEQ ID No. 5 or SEQ ID No. 7, or and also their functional variants, analogues or derivatives thereof; having from 50 to 100% homology based on the corresponding amino acid sequence, are expressed in a prokaryotic or eukaryotic host organism which is able to synthesize biotin, this organism is cultured and the synthesized biotin is used directly after separating off the biomass or after purifying the biotin.

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2. (canceled)

3. (previously amended) A process as claimed in claim 1, wherein an organism selected from the group of the genera Escherichia, Citrobacter, Serratia, Klebsiella, Salmonella, Pseudomonas, Comamonas, Acinetobacter, Azotobacter, Chromobacterium, Bacillus, Clostridium, Arthrobacter, Corynebacterium, Brevibacterium, Lactococcus, Lactobacillus, Streptomyces, Rhizobium, Agrobacterium, Staphylococcus, Rhodotorula, Sporobolomyces, Yarrowia, Schizosaccharomyces or Saccharomyces is used as the host organism.

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4. (previously amended) A process as claimed in claim 1, wherein a

regulation-defective biotin mutant is used as the host organism.

5. (previously amended) A process as claimed in claim 1, wherein at least one copy of the genes having the sequences SEQ ID No.1, SEQ ID No. 3, SEQ ID No. 5 and SEQ ID No. 7 as claimed in claim 1 is expressed in a prokaryotic or eukaryotic host organism either alone or together with one or more copies of at least one further biotin gene selected from the group bioA, bioB, bioF, bioC, bioD, bioH, bioP, bioW, bioX, bioY or bioR.

6. (previously amended) A process as claimed in claim 1, wherein at least one copy of the genes having the sequences SEQ ID No.1, SEQ ID No. 3, SEQ ID No. 5 and SEQ ID No. 7 as claimed in claim 1 is expressed in a prokaryotic or eukaryotic host organism either alone or, on a shared vector or on separate vectors, together with one or more copies at least one further biotin gene selected from the group bioA, bioB, bioF, bioC, bioD, bioH, bioP, bioW, bioX, bioY or bioR.

7. (currently amended) A gene construct which comprises an S-adenosylmethionine synthase gene, having the sequence SEQ ID No. 1, and at least one further biotin biosynthesis gene bioS1, bioS2 or bioS3, having the sequences SEQ ID No. 3, SEQ ID No. 5 and SEQ ID No. 7, or and also their functional variants, analogues or derivatives, which have from 50 to 100% homology, based on the corresponding amino acid sequence, and which is functionally linked to one or

*C2* more regulatory signals for the purpose of increasing gene expression and/or protein expression and/or whose natural regulation has been switched off.

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8. (original) A gene construct as claimed in claim 7, which has been inserted into a vector which is suitable for expressing the gene in a prokaryotic or eukaryotic host organism.

9. (previously amended) A gene construct as claimed in claim 7, wherein the genes having the sequences SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5 and SEQ ID No. 7, and also their functional variants, analogues or derivatives, are present in several copies in the gene construct.

10. (previously amended) A gene construct as claimed in claim 7, wherein the S-adenosylmethionine synthase gene, SEQ ID No. 1, and at least one further biotin biosynthesis gene bioS1, bioS2 or bioS3, having the sequences SEQ ID No. 3, SEQ ID No. 5 and SEQ ID No. 7, and also their functional variants, analogues or derivatives, as claimed in claim 7, are present in the gene construct or vector together with one or more copies of at least one further gene selected from the group bioA, bioB, bioF, bioC, bioD, bioH, bioP, bioW, bioX, bioY or bioR.

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11. (previously amended) An organism which comprises a gene construct as claimed in

claim 7.

12. (canceled)

13. (original) The use of the bioS3 gene, having the sequence SEQ ID No. 7, or of its functional variants, analogues or derivatives, either alone or in combination with at least one further gene selected from the group S-adenosylmethionine synthase gene, bioS1, bioS2, bioA, bioB, bioF, bioC, bioD, bioH, bioP, bioW, bioX, bioY or bioR, for producing biotin.

14. (previously amended) The use of a gene construct as claimed in claim 7 for producing biotin.

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15. (newly added) A process for producing biotin wherein an S-adenosylmethionine synthase gene having the sequence SEQ ID No. 1, and at least one biotin biosynthesis gene selected from the group consisting of O-acetylserine sulfohydrolase A, O-acetylserine sulfohydrolase B,  $\beta$ -cystathionase, nifS, and their prokaryotic and eukaryotic homologues, are expressed in a prokaryotic or eukaryotic host organism which is able to synthesize biotin, this organism is cultured and the synthesized biotin is used directly after separating off the biomass or after purifying the biotin.

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